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Respiratory distress caused by radioiodine therapy in patients with differentiated thyroid cancer

Seigo KINUYA, Kunihiko YOKOYAMA, Takatoshi MICHIGISHI and Norihisa TONAMI

Department of Biotracer Medicine, Kanazawa University Graduate School of Medical Sciences and Department of Nuclear Medicine, Kanazawa University Hospital

Respiratory distress accompanied by stridor is an uncommon complication of ^{131}I radioiodine therapy for differentiated thyroid cancer that occurs within 48 hours of treatment. This report presents three cases with papillary thyroid carcinoma in which ^{131}I therapy caused this acute complication. One of them had no apparent risk for this complication such as the existence of remnant thyroid tissue or laryngeal problems before the treatment. These cases remind physicians that ^{131}I therapy is not a simple, riskless procedure.

Key words: ^{131}I, thyroid cancer, neck edema, respiratory distress, complication

INTRODUCTION

RADIOACTIVE iodine (^{131}I) therapy for differentiated thyroid cancer is generally considered to be a treatment that rarely causes serious complications. Common acute complications of ^{131}I therapy are so-called radiation sickness and radiation sialadenitis that can be easily handled by medications such as antiemetics and antiinflammatory drugs.[1] Radiation thyroiditis may occur in patients with remnant thyroid tissue, characterized by pain and swelling in the neck,[1] that may rarely swell enough to cause airway obstruction.[1] It typically occurs 3 or 4 days later when the radiation dose delivered to the thyroid remnant amounts to about 500 cGy.[1] Neck edema is a less common problem that is distinct from radiation thyroiditis, occurring within 48 hours after ^{131}I administration and accompanied by stridor.[1,2] We recently experienced three patients with this complication: one of them did not have remnant thyroid tissue or cervical lesions according to pre-therapeutic evaluation with ultrasonography (US) and x-ray computed tomography (x-CT). In order to emphasize that ^{131}I therapy may cause this type of serious problem in any patient, we report these cases here.

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For reprint contact: Seigo Kinuya, M.D., Department of Biotracer Medicine, Kanazawa University Graduate School of Medical Sciences, 13–1 Takaramachi, Kanazawa, Ishikawa 920–8640, JAPAN.

E-mail: kinuya@med.kanazawa-u.ac.jp

CASE REPORTS

Case 1

A 55-year-old woman who underwent total thyroidectomy and bilateral cervical lymph node dissection for papillary carcinoma of the thyroid 10 years earlier was referred to our department for ^{131}I therapy because of multiple pulmonary metastases (Fig. 1A). She had suffered from snoring for 1 year and hoarseness for 6 months. Laryngoscopic evaluation revealed bilateral recurrent laryngeal nerve paralysis (Fig. 1B). Recurrent lesions were found adjacent to the trachea in x-CT (Fig. 1C). Bronchoscopy performed to examine the tracheal mucosa indicated no tumoral invasion to the mucosa despite the compression of the wall 2 cm below the glottis. She received 3.7 GBq of ^{131}I after 2-week restriction of dietary iodine intake and withdrawal of liothyronine. The free T3 (FT3) was 1.23 pg/m*l* (normal, 2.7 to 5.9 pg/m*l*), free T4 (FT4) was 0.23 ng/d*l* (normal, 0.78 to 2.11 ng/d*l*), thyroid stimulating hormone (TSH) was 168.70 μU/m*l* (normal, 0.25 to 5.5 μU/m*l*), thyroglobulin was 3590.6 ng/m*l*, and anti-thyroglobulin antibody was 12.4 IU/m*l*. She complained of discomfort in the neck approximately 18 hours after the administration. Twelve hours later, she developed difficulty in breathing. Around 36 hours after the ^{131}I administration, she showed cyanosis with oxygen saturation of 55%. Then, the respiratory distress was relieved by endotracheal intubation. On the next day, tracheostomy was performed. Laryngoscopy demonstrated that the glottis was edematous and the airway was completely obstructed

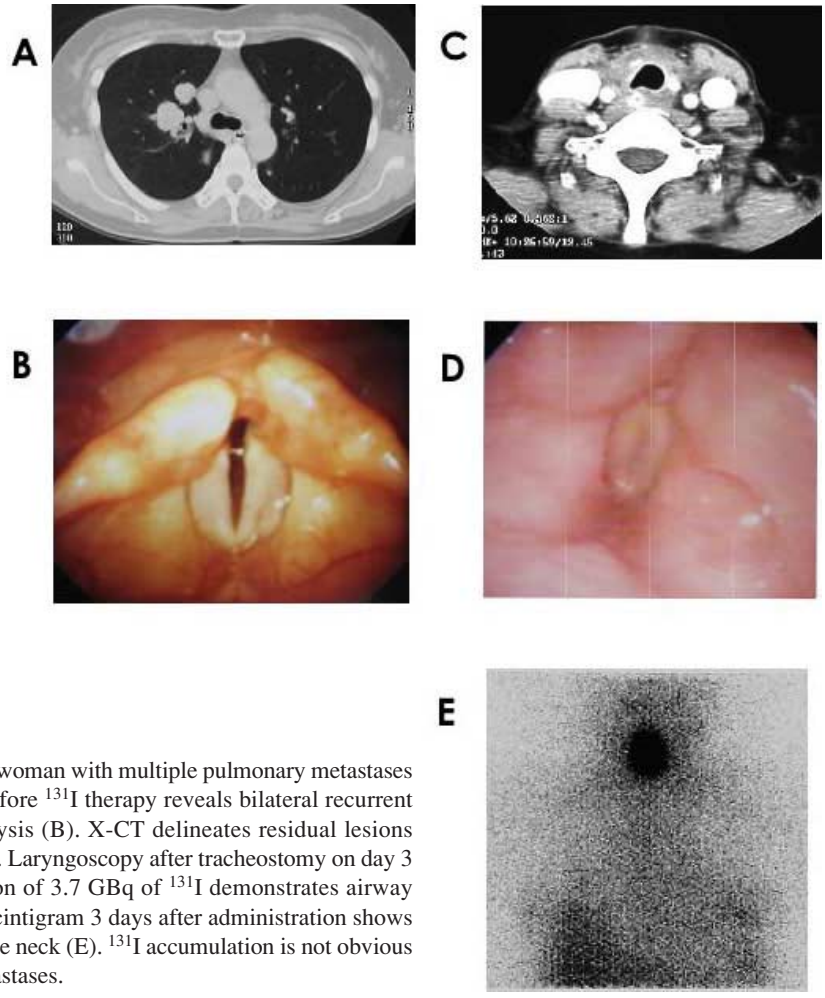


Fig. 1 A 55-year-old woman with multiple pulmonary metastases (A). Laryngoscopy before ^{131}I therapy reveals bilateral recurrent laryngeal nerve paralysis (B). X-CT delineates residual lesions around the trachea (C). Laryngoscopy after tracheostomy on day 3 after the administration of 3.7 GBq of ^{131}I demonstrates airway obstruction (D). ^{131}I scintigram 3 days after administration shows ^{131}I accumulation in the neck (E). ^{131}I accumulation is not obvious in the pulmonary metastases.

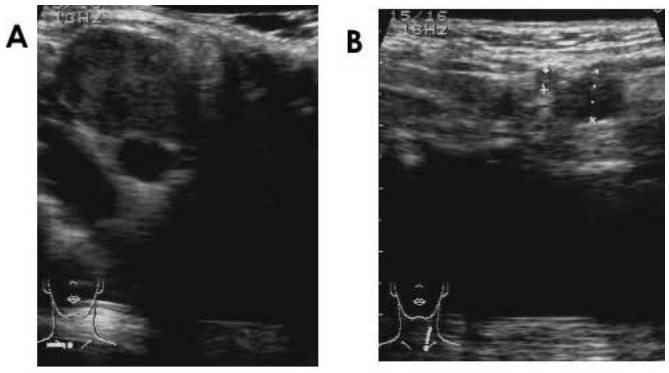
(Fig. 1D). ^{131}I scintigram 3 days after administration showed ^{131}I accumulation in the neck (Fig. 1E). ^{131}I accumulation was not observed in the pulmonary metastases, suggesting that radioactivity in the neck was derived from ^{131}I accumulation in the thyroid bed.

Case 2

A 70-year-old woman underwent right subtotal thyroidectomy and bilateral cervical lymph node dissection for papillary carcinoma of the thyroid 11 years earlier, in which the right recurrent laryngeal nerve was dissected because of tumorous invasion. A metastatic lymph node of 2 cm in diameter was detected in the right supraclavicular region on ultrasonography (US) (Fig. 2A). Remnant left lobe of the thyroid was also observed (Fig. 2B). ^{131}I therapy was planned for the thyroidal ablation, so that the second surgery was performed to dissect the recurrent lymph node and the remnant thyroid tissue. The metastatic lymph node was excised; however, the surgeon failed to remove the residual normal thyroid tissue because it could not be visually detected. Chest x-CT and bone scintigraphy did not show any evidence of pulmonary metastasis or bone metastasis. FT3 was 2.05 pg/m*l*, FT4 was 0.47 ng/d*l*, TSH was 59.29 μU/m*l*, thyroglobulin was 126.6 ng/m*l*, and anti-thyroglobulin antibody was 27.5 IU/m*l* on the day of ^{131}I administration. She received 3.7 GBq of ^{131}I. She felt discomfort in the neck one day after the administration. The anterior neck was swollen, and redness of the skin was observed. Prednisolone of 10 mg was orally given. She started to complain of difficulty in breathing about 36 hours after the ^{131}I administration. Slight stridor was heard several hours later, so that hydrocortisone and a histamine H_1 receptor antagonist were infused intravenously. The symptom resolved in a few hours. ^{131}I scintigram obtained 3 days after the administration demonstrated intense ^{131}I accumulation in the neck (Fig. 2C).

Case 3

A 64-year-old woman underwent subtotal thyroidectomy for papillary thyroid cancer 14 years earlier. Because of multiple pulmonary metastases (Fig. 3A), the remnant thyroid tissue was surgically removed and she was referred to our department for ^{131}I therapy. There was no



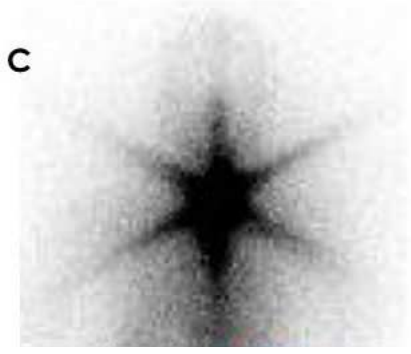


Fig. 2 A 70-year-old woman who underwent right subtotal thyroidectomy and bilateral cervical lymph node dissection for papillary carcinoma of the thyroid 11 years earlier. US shows a metastatic lymph node of 2 cm in diameter in the right supraclavicular region (A) and the remnant left lobe of the thyroid (B). She started to complain of difficulty in breathing about 36 hours after the 3.7 GBq of ^{131}I administration. ^{131}I scintigram 3 days after administration demonstrates intense ^{131}I accumulation in the neck (C).

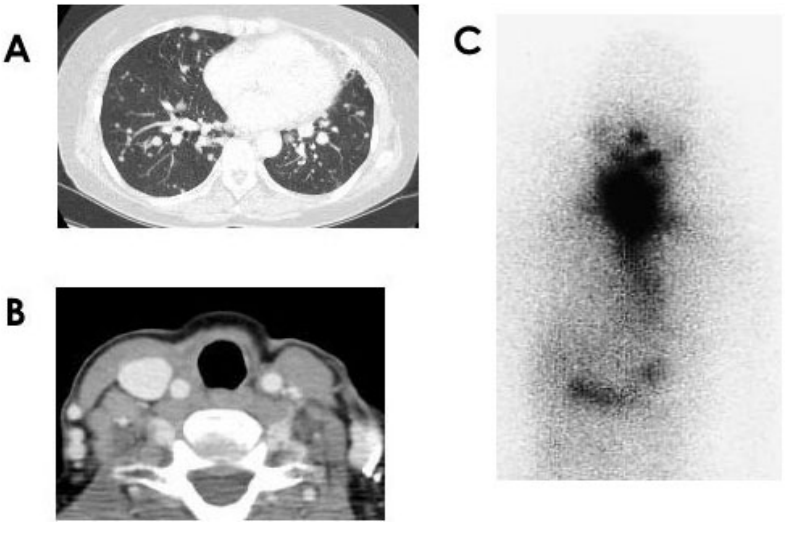


Fig. 3 A 64-year-old with multiple pulmonary metastases (A). No apparent residual lesion or thyroid tissue is observed in x-CT (B) or US. Laryngoscopy showed no abnormal movement of the vocal cords. She started to complain of difficulty in breathing 36 hours after the administration of 5.55 GBq of ^{131}I. ^{131}I scintigram 3 days after administration delineates intense ^{131}I accumulation in the neck (C).

evidence of residual lesions or thyroid tissue in the neck on examinations with US and x-CT (Fig. 3B). Laryngoscopy showed no abnormal movement of the vocal cords. FT3 was <0.7 pg/m*l*, FT4 was <0.20 ng/d*l*, TSH was 124.16 μU/m*l*, thyroglobulin was 5270.0 ng/m*l*, and antithyroglobulin antibody was 35.5 IU/m*l* on the day of ^{131}I administration. She received 5.55 GBq of ^{131}I. Twelve hours after the administration, she started to experience hoarseness and swelling of the neck. She was given 10 mg of prednisolone orally every 12 hours. However, 26 hours after the onset of the symptom, she started to complain of difficulty in breathing. Swelling of the neck was

developing. Hydrocortisone was infused intravenously, and the breathing difficulty gradually subsided in a few hours. ^{131}I scintigram delineated intense ^{131}I accumulation in the neck (Fig. 3C). There was no appreciable ^{131}I uptake in pulmonary metastases.

DISCUSSION

Three of 102 patients undergoing ^{131}I therapy for thyroid cancer in our department experienced respiratory distress in these 4 years. Only a few reports that show a similar complication are available in the literature so far; however, our experience suggests that this early complication may occur more often than is considered by physicians. Furthermore, the important fact shown by the case presented in this report is that this complication may occur in patients with no cervical lesions or remnant thyroid tissue in morphological images. Therefore, physicians must be aware of the possibility that this serious problem may happen in any patient receiving high-dose ^{131}I therapy.

The major factor of respiratory distress observed in these three cases appears to be non-specific neck edema related to irradiation to the remnant thyroid or thyroid bed.[1,2] Case 1 had lesions in the neck and lungs. Because pulmonary accumulation of ^{131}I was not obvious, it would be reasonably considered that the major source of ^{131}I in the neck would be associated with the thyroid bed rather than the recurrent lesions around the trachea. Furthermore, because of the short path-length of beta-rays of ^{131}I and little contribution of gamma-rays to radiation doses to surrounding tissues, it is unlikely that radiation from the thyroid bed directly induced the swelling of the glottis. In case 2, intense ^{131}I accumulation in the neck was surely due to the remnant thyroid tissue. Early onset of the symptom suggested that her symptom was unlikely associated with radiation thyroiditis because the radiation dose to the thyroid was not high enough to typically cause this entity at the time when she complained of it. In case 3, there is little doubt that ^{131}I accumulation in the thyroid bed caused the trouble. Direct effects of radiation on the larynx should not have occurred in this situation because of the aforementioned reasons regarding the physical characteristics of ^{131}I.

All previously reported cases of ^{131}I-induced respiratory distress had remnant thyroid tissue like case 2 in this report to which ^{131}I produced considerable radiation doses.[2] In all of them, the complication appeared within 48 hours.[1,2] Because it is unlikely that the radiation dose to the tissues adjacent to the thyroid in the first 48 hours is high enough to cause tissue edema, some mechanism other than a direct radiation effect on perithyroidal tissues must be involved.[2]

Vocal cord paralysis may occur during ^{131}I therapy for the ablation of the thyroid remnant.[3] This entity may also occur in ^{131}I therapy for thyrotoxicosis.[4–6] In the reported cases, recovery of the vocal cord movement took several months. Rapid recovery in our cases indicates that this mechanism would be hardly responsible for the symptom.

Goolden et al.[2] suggested an allergic reaction as a possible mechanism for the respiratory distress occurring within 48 hours after the ^{131}I administration. That is, release of a variety of degradation products into the circulation induced angioneurotic edema. Rapid symptomatic responses to corticosteroids may support this hypothesis. According to this hypothesis, a histamine H_1 receptor antagonist was used in case 2.

We did not perform tracer studies before the administration of therapeutic dose of ^{131}I in all cases, because of the possible stunning phenomenon of tissues caused by tracer dose of ^{131}I and the fact that a therapeutic dose of ^{131}I often delineates lesions missed with tracer dose scintigraphy.

In summary, three cases in which ^{131}I therapy for papillary thyroid carcinoma caused respiratory distress possibly via an allergic reaction were reported. One of them suffered from this complication despite having no remnant thyroid tissue or cervical lesion and no laryngeal problems before the ^{131}I administration. These cases strongly remind physicians that this type of early complication may occur in patients with any kind of background.

NOTE

These cases were reported in the symposium entitled "Re-evaluation of ^{131}I Radioiodotherapy for Thyroid Diseases" held as a part of the 45th annual meeting of the Japanese Society of Nuclear Medicine in Tokyo, 2005.

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